ARCHITECT®
SYSTEM

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Anti-HCV
REF 1L79
34-4152/R1

Anti-HCV

Customer Service
United States: 1-877-4ABBOTT

Caution: United States Federal Law restricts this device to sale and distribution by or on the order of a physician, or to a clinical laboratory; and use is restricted to by or on the order of a physician.

This package insert must be read carefully before product use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

REF	List Number	REACTION VESSELS	Reaction Vessels
IVD	*In Vitro* Diagnostic Medical Device	SAMPLE CUPS	Sample Cups
2°C 8°C	Store at 2-8°C	SEPTUMS	Septums
LOT	Lot Number	REPLACEMENT CAPS	Replacement Caps
	Expiration Date	SN	Serial Number
	Consult instructions for use	CONTROL NO.	Control Number
		REAGENT LOT	Reagent Lot

See **REAGENTS** section for a full explanation of symbols used in reagent component naming

Abbott Laboratories
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Abbott Park, IL 60064 USA

Printed in USA

NAME

ARCHITECT Anti-HCV

INTENDED USE

The ARCHITECT Anti-HCV assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to hepatitis C virus (anti-HCV) in human adult serum and plasma (potassium EDTA, lithium heparin, and sodium heparin). Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with HCV (state of infection or associated disease not determined) in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis C infection.

Warning: Not intended for use in screening blood, plasma, or tissue donors. The effectiveness of ARCHITECT Anti-HCV for use in screening blood, plasma, or tissue donors has not been established.

Assay performance characteristics have not been established for newborns, infants, children, or populations of immunocompromised or immunosuppressed patients. The user is responsible for establishing their own assay performance characteristics in these populations.

SUMMARY AND EXPLANATION OF THE TEST

The ARCHITECT Anti-HCV assay is for the detection of antibodies to the hepatitis C virus (HCV). Chemiluminescent immunoassays are a variation of the enzyme immunoassay (EIA) principle. Solid phase EIAs, first described in the early 1970s, use antigens and/or antibodies coated on a surface to bind complementary analytes.[1] The bound analyte is detected by a series of antigen-antibody reactions. EIAs are available to identify antigens and antibodies related to viral hepatitis infection. In the ARCHITECT Anti-HCV final reaction, bound acridinylated conjugates are used to generate a chemiluminescent signal.

HCV is a bloodborne virus.[2,3] Serological studies employing EIAs for detection of antibodies to recombinant antigens of HCV have established HCV as the cause of most bloodborne[4-6] as well as community-acquired[1c] non-A, non-B hepatitis. The presence of anti-HCV indicates that an individual may have been infected with HCV, may harbor infectious HCV, and/or may be capable of transmitting HCV infection.[11]

Although the majority of infected individuals may be asymptomatic, HCV infection may develop into chronic hepatitis, cirrhosis, and/or increased risk of hepatocellular carcinoma.[12-15] The implementation of blood donation screening for anti-HCV by EIAs has led to a marked decline in the risk of transfusion-transmitted hepatitis.[16,17]

ARCHITECT Anti-HCV has been designed to detect antibodies to putative structural and nonstructural proteins of the HCV genome. The relationship between the recombinant HCV proteins in ARCHITECT Anti-HCV and the putative structural and nonstructural proteins of the HCV genome is depicted below.[18]

- HCr43: The HCr43 protein is expressed in *Escherichia coli* (*E. coli*) and is composed of two noncontiguous coding regions of the HCV genome sequence. The first region represents amino acids 1192 to 1457 (33c) of the HCV sequence. The second of the two regions represents amino acids 1 to 150 (core) of the HCV sequence. Because of the similarity of the genomic organization of the flaviviruses, it is suggested that the first sequence is from the NS3 coding region and the second sequence is from the core coding region of HCV.
- c100-3: The c100-3 antigen is a recombinant HCV protein expressed in *Saccharomyces cerevisiae* (yeast). The genomic organization of flaviviruses suggests that the cloned sequence is contained within the putative nonstructural (NS3 and NS4) regions of HCV. The c100-3 protein is a chimeric fusion protein with 154 amino acids of human superoxide dismutase (hSOD), five linker amino acids, amino acids number 1569 to 1931 of the HCV polyprotein, and the additional five amino acid linker at the carboxyl terminus.

Hepatitis C antigens HCr43 and c100-3 are prepared under US license by Chiron Corporation under a shared manufacturing agreement. The ARCHITECT Anti-HCV assay is manufactured under contract agreement from Ortho Diagnostic Systems and Chiron Corporation.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Anti-HCV assay is a two-step immunoassay for the qualitative detection of anti-HCV in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample, recombinant HCV antigen coated paramagnetic microparticles, and assay diluent are combined. Anti-HCV present in the sample binds to the HCV coated microparticles. After washing, anti-human IgG/IgM acridinium-labeled conjugate is added in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A relationship exists between the amount of anti-HCV in the sample and the RLUs detected by the ARCHITECT *i* optical system.

The presence or absence of anti-HCV in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active ARCHITECT Anti-HCV calibration curve. If the chemiluminescent signal of the sample is greater than or equal to the cutoff signal, the sample is considered reactive for anti-HCV.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100/500 Tests

NOTE: Reagent Kit configuration varies based on order.

ARCHITECT Anti-HCV Reagent Kit (No. 1L79)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL/27.0 mL) HCV antigen (recombinant *E. coli*, recombinant yeast) coated microparticles in MES buffer. Minimum concentration: 0.14% solids. Preservatives: antimicrobial agents.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL/25.3 mL) murine anti-human IgG/IgM acridinium-labeled conjugate in MES buffer with protein (bovine) additive (152 µM) and surfactant. Minimum concentration: (IgG) 8 ng/mL/ (IgM) 0.8 ng/mL. Preservatives: antimicrobial agents.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (10.0 mL/50.9 mL) anti-HCV assay diluent containing TRIS buffer with protein (goat) additive (102.6 g/L) and surfactant. Preservative: ProClin® 300.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

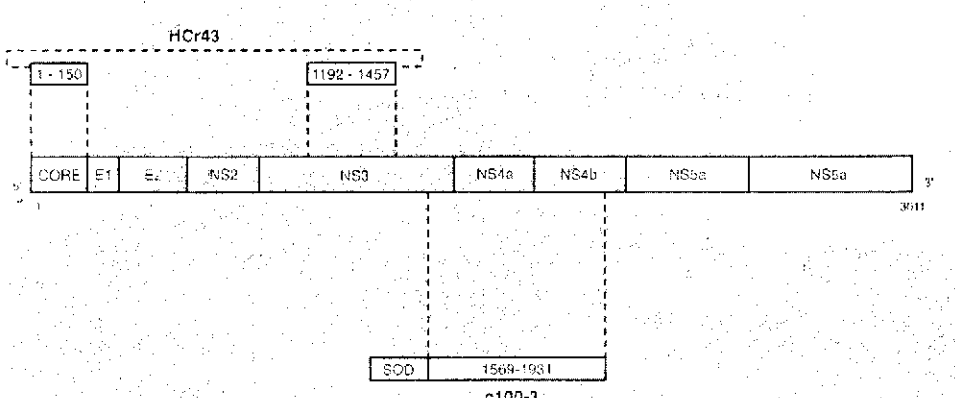
- **PRE-TRIGGER SOLUTION** Pre-trigger solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger solution containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash buffer containing phosphate buffered saline solution. Preservative: antimicrobial agent.



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WARNINGS AND PRECAUTIONS

For *In Vitro* Diagnostic Use.

Safety Precautions

- **CAUTION: This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.[19] Biosafety Level 2[20] or other appropriate biosafety practices[21,22] should be used for materials that contain or are suspected of containing infectious agents.**
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagents beyond the expiration date.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Before loading the ARCHITECT Anti-HCV Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
  - **To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.**
  - **When handling conjugate vials, change gloves that have contacted human plasma/serum, since introduction of human IgG/IgM will result in a neutralized conjugate.**
  - Before placing the septum on an uncapped reagent bottle, squeeze the septum in half to confirm that the slits are open. If the slits appear sealed, continue to gently squeeze the septum to open the slits.
  - *Once a septum* has been placed on the reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- 2°C to 8°C The ARCHITECT Anti-HCV Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, the reagents are stable until the expiration date.
- The ARCHITECT Anti-HCV Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, initiate a scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT Anti-HCV assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* System Assay CD ROM before performing the assay. For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

- The following specimen tube types were verified for use with the ARCHITECT Anti-HCV assay:

Glass	Plastic
• Serum • Serum separator	• Serum • Serum separator • Lithium heparin plasma separator • Sodium heparin • Dipotassium EDTA

- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT Anti-HCV assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed
  - obvious microbial contamination
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum and plasma.
- **For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.** Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at > 10,000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
  - they contain fibrin, red blood cells, or other particulate matter or
  - they were frozen and thawed.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.
- Transfer clarified specimen to a sample cup or secondary tube for testing.

Storage

- Specimens may be stored on or off the clot, red blood cells, or separator gel for
  - up to 3 days at room temperature (study performed at 20 to 23°C) or
  - up to 7 days at 2-8°C.
- If testing will be delayed more than 3 days for specimens stored at room temperature or more than 7 days for specimens stored at 2-8°C, remove serum or plasma from the clot, red blood cells, or separator gel and store at -20°C or colder.
- Avoid more than three freeze/thaw cycles.

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Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped ambient, at 2-8°C (wet ice), or frozen (dry ice). Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided:

- 1L79 ARCHITECT Anti-HCV Reagent Kit

Materials Required but not Provided:

- ARCHITECT *i* System
- ARCHITECT *i* System Assay CD-ROM
- 1L79-01 ARCHITECT Anti-HCV Calibrator
- 1L79-10 ARCHITECT Anti-HCV Controls (or other control material)
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUMS**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the specified volumes.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT Anti-HCV Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Handling Precautions** section of this package insert.
- Load the ARCHITECT Anti-HCV Reagent Kit on the ARCHITECT *i* System.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and the positive control and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
  - Use the following instructions to order a negative control (nonreactive for anti-HCV):
    - Order a negative control as a patient specimen, not as a Control.
    - Manually verify the validity of the negative control every time it is run. Because the control is run as a patient specimen, a result will not be flagged by the ARCHITECT *i* System if it is outside the acceptable control range.
  - To troubleshoot control values that fall outside the control range, refer to the ARCHITECT System Operations Manual, Section 10.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
  - Priority: 70 µL for first anti-HCV test plus 20 µL for each additional anti-HCV test from the same sample cup.
  - ≤ 3 hours onboard: 150 µL for the first anti-HCV test plus 20 µL for each additional anti-HCV test from the same sample cup.
  - > 3 hours on board: Replace with a fresh sample (patient specimens, controls, and calibrator).
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrator and controls.
  - ARCHITECT Anti-HCV Calibrator and Controls must be mixed by gentle inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT Anti-HCV Calibrator and Controls, hold the bottles **vertically** and dispense 5 drops of the calibrator or 6 drops of each control into each respective sample cup.
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedure

- Specimens cannot be diluted for the ARCHITECT Anti-HCV assay.

Calibration

- To perform a calibration, test ARCHITECT Anti-HCV Calibrator 1 in triplicate. The calibrator should be priority loaded.
- A single sample of each control level must be tested to evaluate the assay calibration.
  - Order controls as described above.
  - Ensure that assay control values are within the ranges specified in the control package insert.
- Once an ARCHITECT Anti-HCV calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.

QUALITY CONTROL PROCEDURES

The ARCHITECT Anti-HCV Controls are in a serum matrix made from recalcified plasma. The user should provide alternate control material for plasma when necessary.

The recommended control requirement for the ARCHITECT Anti-HCV assay is that a single sample of each control level be tested once every 24 hours each day of use. Additional controls may be tested in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Control values must be within the ranges specified in the control package insert. If a control result is out of its specified range, any test results generated since the last acceptable control results must be evaluated to determine if test results may have been adversely affected. Adversely affected test results are invalid, and these samples must be retested. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

RESULTS

Calculation

- The ARCHITECT *i* System calculates the cutoff RLU from the mean chemiluminescent signal of three Anti-HCV Calibrator 1 replicates and stores the result. The cutoff RLU is determined by multiplying the Anti-HCV Calibrator 1 mean RLU by 0.074.

  Cutoff RLU = Calibrator 1 Mean RLU x 0.074
- The ARCHITECT *i* System calculates a result based on the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

  S/CO = Sample RLU/Cutoff RLU ratio

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

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Interpretation of Results

Initial ARCHITECT Anti-HCV Results			
Initial Result (S/CO)	**Instrument Flag**	**Interpretation**	**Retest Procedure**
≥ 1.00	REACTIVE	Reactive	No retest required.
0.80 to 0.99	GRAYZONE	Grayzone	Retest in duplicate.
0.00 to 0.79	NONREACTIVE	Nonreactive	No retest required.

ARCHITECT Anti-HCV Results			
Initial Result	**Retest Result**	**Result**	**Interpretation**
Reactive	No retest required.	**Reactive**	Presumptive evidence of antibodies to HCV; follow CDC recommendations[23] for supplemental testing.
Grayzone	Both of the duplicate retests are reactive.	**Reactive**	Presumptive evidence of antibodies to HCV; follow CDC recommendations[23] for supplemental testing.
	One or both of the duplicate retests are repeatedly in the grayzone or one retest is reactive and the other nonreactive.	**Equivocal**	Antibodies to HCV may or may not be present; another specimen should be obtained from the individual for further testing or follow CDC recommendations[23] for supplemental testing.
	Both of the duplicate retests are nonreactive.	**Nonreactive**	Antibodies to HCV not detected; does not exclude the possibility of exposure to HCV.
Nonreactive	No retest required.	**Nonreactive**	Antibodies to HCV not detected; does not exclude the possibility of exposure to HCV.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, results should be used in conjunction with patient history and other hepatitis markers for diagnosis of acute and chronic infection.
- Current methods for the detection of antibodies to HCV may not detect all infected individuals. A nonreactive test result does not exclude the possibility of exposure to HCV.
- Nonreactive test results in individuals with prior exposure to HCV may be due to antibody levels being below the detection limit of this assay or to lack of antibody reactivity to the recombinant antigens used in this assay.
- Immunocompromised patients who have HCV may produce levels of antibody below the sensitivity of this assay and may not be detected as positive.
- The affinity or avidity differences of anti-human IgG/IgM for anti-HCV have not been determined with this assay. Therefore, there may not be a demonstration of a significant increase in antibody level between acute and convalescent specimens for a patient in the late acute stage of infection when IgM antibodies are decreasing.
- Results obtained with the ARCHITECT Anti-HCV assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- Assay performance characteristics have not been established for newborns, infants, children, or populations of immunocompromised or immunosuppressed patients.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays.[24] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- A reactive anti-HCV result does not exclude co-infection by another hepatitis virus.
- The magnitude of an ARCHITECT Anti-HCV assay result cannot be correlated to an end point titer.
- Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert for specimen limitations.

EXPECTED RESULTS

Due to geographic locations or demographics, assay results obtained in individual laboratories may vary from data presented.

Of the 2027 specimens tested in the ARCHITECT Anti-HCV clinical study, 1310 (64.63%) were from individuals with increased risk of HCV infection. All 1310 were at risk for HCV due to lifestyle, behavior, occupation, or a known exposure event but were asymptomatic and reported no current signs or symptoms of hepatitis. Testing of these specimens was performed at three clinical sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

The asymptomatic population (n=1310) consisted of the following race/ethnic groups:

- 589 (44.96%) Caucasian
- 522 (39.85%) African-American
- 165 (12.60%) Hispanic
- 10 (0.76%) Asian
- 9 (0.69%) American Indian/Alaska Native
- 15 (1.15%) Other

The 1310 specimens from the asymptomatic population were obtained from the following collection locations:

- 707 (53.97%) from Galveston, TX
- 185 (14.12%) from High Point, NC
- 103 (7.86%) from Plymouth, MA
- 76 (5.80%) from Colton, CA
- 64 (4.89%) from Dallas, TX
- 56 (4.27%) from St. Petersburg, FL
- 56 (4.27%) from Miami, FL
- 44 (3.36%) from Denver, CO
- 19 (1.45%) from Chicago, IL

A total of 237 (18.09%) of the specimens in the asymptomatic population were reactive in the ARCHITECT Anti-HCV assay. The number of ARCHITECT Anti-HCV reactive results observed for the asymptomatic population at each collection location was:

- 132 of 707 (18.67%) from Galveston, TX
- 10 of 185 (5.41%) from High Point, NC
- 32 of 103 (31.07%) from Plymouth, MA
- 1 of 76 (1.32%) from Colton, CA
- 15 of 64 (23.44%) from Dallas, TX
- 10 of 56 (17.86%) from Miami, FL
- 10 of 56 (17.86%) from St. Petersburg, FL
- 13 of 44 (29.55%) from Denver, CO
- 14 of 19 (73.68%) from Chicago, IL

Of the 1310 specimens, 864 (65.95%) were female and 446 (34.05%) were male. The age was not reported for three specimens. Of the remaining 1307 specimens, the mean age was 40 years (age range: 18 to 73 years). The distribution of ARCHITECT Anti-HCV reactive, equivocal, and nonreactive results among the asymptomatic population by age and gender (n=1307) is summarized in the following table.

Age Group (years)	Gender	ARCHITECT Anti-HCV Result			Total
		Reactive n (%)	Equivocal n (%)	Nonreactive n (%)	
0-17	F	0 (0.00)	0 (0.00)	0 (0.00)	0
	M	0 (0.00)	0 (0.00)	0 (0.00)	0
18-29	F	12 (5.58)	1 (0.47)	202 (93.95)	215
	M	8 (8.99)	0 (0.00)	81 (91.01)	89
30-39	F	15 (7.21)	1 (0.48)	192 (92.31)	208
	M	18 (18.56)	1 (1.03)	78 (80.41)	97
40-49	F	48 (18.25)	0 (0.00)	215 (81.75)	263
	M	55 (37.16)	0 (0.00)	93 (62.84)	148
50-59	F	26 (18.98)	0 (0.00)	111 (81.02)	137
	M	47 (51.09)	0 (0.00)	45 (48.91)	92
60-69	F	1 (3.03)	0 (0.00)	32 (96.97)	33
	M	4 (25.00)	0 (0.00)	12 (75.00)	16
70-79	F	1 (16.67)	0 (0.00)	5 (83.33)	6
	M	1 (33.33)	0 (0.00)	2 (66.67)	3
Total		236 (18.06)	3 (0.23)	1068 (81.71)	1307†

†Age was not reported for three subjects.

SPECIFIC PERFORMANCE CHARACTERISTICS

Assay results obtained in individual laboratories may vary from data presented.

Precision

- The ARCHITECT Anti-HCV assay is designed to have a Total CV of ≤ 10% for the ARCHITECT Anti-HCV Positive Control, a high negative panel targeted to 0.80 S/CO, and a low positive panel targeted to 1.20 S/CO.

System Reproducibility

A five-day precision study was performed for the ARCHITECT Anti-HCV assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP15-A2.[25] Testing was conducted at three clinical sites using three lots each of ARCHITECT Anti-HCV Reagents, Calibrator, and Controls per site. Two levels of controls and panels were assayed in replicates of four at two separate times of day for 5 days. The data are summarized in the following table.

Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)		Precision with Additional Component of Between-Site		Precision with Additional Component of Between-Lot		Precision with Additional Components of Site and Lot (Overall)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	360	3.68	0.118	3.2	0.122	3.3	0.127	3.5	0.136	3.7	0.136	3.7	0.136	3.7
High Negative Panel	360	0.77	0.045	5.9	0.048	6.2	0.048	6.2	0.049	6.4	0.073	9.5	0.074	9.5
Low Positive Panel	360	1.15	0.064	5.6	0.066	5.7	0.066	5.8	0.069	6.0	0.106	9.2	0.107	9.3
Negative Control	360	0.12	0.006	NA	0.006	NA	0.007	NA	0.010	NA	0.055	NA	0.055	NA

NA = not applicable

Within-Laboratory Precision

A 20-day precision study was performed for the ARCHITECT Anti-HCV assay based on guidance from the CLSI document EP5-A2.[26] Testing was conducted at Abbott Laboratories using three ARCHITECT Anti-HCV assay reagent lots, three calibrator lots, one control lot, and two instruments. Two levels of controls and panels were assayed in replicates of two at two separate times of day for 20 different days. The data are summarized in the following table.

Instrument	Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)	
				SD	%CV	SD	%CV	SD	%CV
1	Positive Control	240	3.54	0.088	2.5	0.096	2.7	0.110	3.1
	High Negative Panel	240	0.77	0.026	3.4	0.028	3.7	0.028	3.7
	Low Positive Panel	240	1.13	0.039	3.5	0.041	3.6	0.041	3.6
	Negative Control	240	0.20	0.013	NA	0.037	NA	0.071	NA
2	Positive Control	240	3.52	0.100	2.8	0.100	2.8	0.117	3.3
	High Negative Panel	240	0.76	0.029	3.8	0.029	3.8	0.033	4.3
	Low Positive Panel	240	1.13	0.041	3.6	0.041	3.6	0.043	3.8
	Negative Control	240	0.17	0.009	NA	0.024	NA	0.031	NA

NA = not applicable

Clinical Performance

A prospective multi-center study was conducted to evaluate the ability of the ARCHITECT Anti-HCV assay to detect anti-HCV antibodies in a group of individuals that would normally be tested in a clinical situation. Of the 2027 specimens tested in the ARCHITECT Anti-HCV clinical study, 1310 specimens were obtained from individuals with increased risk of HCV infection due to lifestyle, behavior, occupation, disease state, or a known exposure event and 717 specimens were obtained from individuals exhibiting signs and symptoms of hepatitis infection.

The specimen population (n=2027) consisted of the following race/ethnic groups:

- 1035 (51.06%) Caucasian
- 631 (31.13%) African-American
- 294 (14.50%) Hispanic
- 30 (1.48%) Asian
- 12 (0.59%) American Indian/Alaska Native
- 25 (1.23%) Other

The 2027 specimens from the specimen population were obtained from the following collection locations:

- 757 (37.35%) from Galveston, TX
- 345 (17.02%) from Plymouth, MA
- 185 (9.13%) from High Point, NC
- 181 (8.93%) from Chicago, IL
- 140 (6.91%) from Denver, CO
- 126 (6.22%) from Dallas, TX
- 118 (5.82%) from Colton, CA
- 94 (4.64%) from Miami, FL
- 81 (4.00%) from St. Petersburg, FL

Of the 2027 specimens, 1126 (55.55%) were female and 901 (44.45%) were male. The age was not reported for three specimens. Of the remaining 2024 specimens, the mean age was 41 years (age range: 18 to 83 years). The HCV status was determined for each specimen using the comparator anti-HCV assay and, as indicated, supplemental assays (Chiron RIBA® HCV 3.0 Strip Immunoblot Assay [SIA] and Roche COBAS AMPLICOR™ Hepatitis C Virus [HCV] Test v2.0). During the clinical study, all comparator and supplemental testing was performed following manufacturers' instructions. Each specimen was also tested using the ARCHITECT Anti-HCV assay at the three clinical sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

Results by Specimen Classification

Following testing with the comparator anti-HCV assay and supplemental testing, where indicated, 2027 specimens were assigned an HCV status of *HCV Infected*, *HCV Not Determined*, or *HCV Not Infected* based on the final results obtained with the comparator or supplemental assays according to the following algorithm.

Comparator Anti-HCV Assay Final Result	Supplemental Assay Final Results		HCV Status[23]
Nonreactive	--		Not Infected[a]
	Chiron RIBA HCV 3.0 SIA	Roche COBAS AMPLICOR HCV Test v2.0	
Reactive	Positive	--	Infected[b]
Reactive	Indeterminate or Negative	Positive	Infected[b]
Reactive	Indeterminate or Negative	Equivocal	Not Determined[a]
Reactive	Indeterminate or Negative	Negative	Not Infected[a]
Equivocal	Positive	--	Infected[b]
Equivocal	Indeterminate or Negative	Positive	Infected[b]
Equivocal	Indeterminate or Negative	Equivocal	Not Determined[a]
Equivocal	Indeterminate or Negative	Negative	Not Infected[a]

[a] A negative test result does not exclude the possibility of exposure to HCV.

[b] State of associated disease Not Determined.

[c] Indicates active HCV infection.

[2] HCV status cannot be determined.

-- = not performed

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Comparison of Results

The following table compares the ARCHITECT Anti-HCV assay results with HCV status for the increased risk and signs and symptoms populations. The increased risk population was ranked according to the risk of HCV infection in study subjects. The risk of HCV infection was ranked based on a clinical evaluation of the likelihood of acquiring HCV through each mode of transmission; the mode of transmission was ranked higher if the likelihood of acquiring HCV was greater.[27] Each specimen was assigned only one risk (the highest ranked). The status of HCV infection was assigned according to the algorithm presented in the table in the previous section. Of the 2027 specimens tested, the status of 616 specimens was *HCV Infected*. The status of 1411 specimens was *HCV Not Infected*. No specimens had the status *HCV Not Determined*. The data are summarized in the following table.

	HCV Status						
	HCV Infected			Not HCV Infected			
Specimen Population	Reactive n (%)	Equivocal n (%)	Nonreactive n (%)	Reactive n (%)	Equivocal n (%)	Nonreactive n (%)	Total n (%)
Individuals with increased risk of HCV infection							
Recipients of clotting factor concentrates prior to 1987	1 (0.05)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (0.10)	3 (0.15)
Users of injecting drugs	97 (4.79)	0 (0.00)	0 (0.00)	8 (0.39)	0 (0.00)	85 (4.19)	190 (9.37)
Multiple sex partners	53 (2.61)	0 (0.00)	1 (0.05)	6 (0.30)	1 (0.05)	587 (28.96)	648 (31.97)
Transfusion recipient prior to July 1992 or received blood from donor later to be found HCV positive	18 (0.89)	0 (0.00)	0 (0.00)	2 (0.10)	0 (0.00)	22 (1.09)	42 (2.07)
Perinatal exposure; mother was infected with hepatitis C	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	3 (0.15)	3 (0.15)
Men who have sex with men	1 (0.05)	0 (0.00)	0 (0.00)	2 (0.10)	0 (0.00)	11 (0.54)	14 (0.69)
Needle stick or mucosal exposure on the job	13 (0.64)	0 (0.00)	0 (0.00)	3 (0.15)	2 (0.10)	252 (12.43)	270 (13.32)
Other*: Household contact with hepatitis C infected individual and/or intranasal cocaine user	31 (1.53)	0 (0.00)	0 (0.00)	2 (0.10)	0 (0.00)	107 (5.28)	140 (6.91)
Individuals with signs and symptoms of a hepatitis infection	400 (19.73)	0 (0.00)	1 (0.05)	7 (0.35)	0 (0.00)	309 (15.24)	717 (35.37)
Total	614 (30.29)	0 (0.00)	2 (0.10)	30 (1.48)	3 (0.15)	1378 (67.98)	2027 (100.00)

* Not based on CDC recommendations

Percent Agreement

The positive percent agreement between the ARCHITECT Anti-HCV assay results and the *HCV Infected* status for the overall population (n = 2027) was 99.68% (614/616, with a 95% confidence interval of 98.83% to 99.96%). Among the specimens with *HCV Infected* status, there were 0.00% (0/616) equivocal results by ARCHITECT Anti-HCV assay (95% confidence interval is 0.00% to 0.60%). The negative percent agreement between the ARCHITECT Anti-HCV assay results and the *HCV Not Infected* status for the overall population was 97.66% (1378/1411, with a 95% confidence interval of 96.73% to 98.38%). Among the specimens with *HCV Not Infected* status, there were 0.21% (3/1,411) equivocal results by ARCHITECT Anti-HCV assay (95% confidence interval is 0.04% to 0.62%).

The table below summarizes the positive percent agreement and negative percent agreement data for individuals with increased risk of HCV infection by hepatitis risk group.

Hepatitis C Ranked Risk Group	Positive Percent Agreement % (x/n)[b]	95% Confidence Interval	Negative Percent Agreement % (x/n)[b]	95% Confidence Interval
Recipients of clotting factor concentrates prior to 1987	100.00 (1/1)	2.50 - 100.00	100.00 (2/2)	15.81 - 100.00
Users of injecting drugs	100.00 (97/97)	96.27 - 100.00	91.40 (85/93)	83.75 - 96.21
Multiple sex partners	98.15 (53/54)	90.11 - 99.95	98.82 (587/594)	97.59 - 99.52
Transfusion recipient prior to July 1992 or received blood from donor later to be found HCV positive	100.00 (18/18)	81.47 - 100.00	91.67 (22/24)	73.00 - 98.97
Perinatal exposure; mother was infected with hepatitis C	NA (0/0)	NA	100.00 (3/3)	29.24 - 100.00
Men who have sex with men	100.00 (1/1)	2.50 - 100.00	84.62 (11/13)	54.55 - 98.08
Needle stick or mucosal exposure on the job	100.00 (13/13)	75.29 - 100.00	98.05 (252/257)	95.52 - 99.37
Other*: Household contact with hepatitis C infected individual and/or intranasal cocaine user	100.00 (31/31)	88.78 - 100.00	98.17 (107/109)	93.53 - 99.78
Total	99.53 (214/215)	97.44 - 99.99	97.63 (1069/1095)	96.54 - 98.44

* Not based on CDC recommendations

[b] x = the number of reactive (or nonreactive) ARCHITECT Anti-HCV results that were in agreement with the HCV status as determined by comparator or supplemental testing;
n = the total number of *HCV Infected* status (or *HCV Not Infected* status) results as determined by comparator or supplemental testing.

Positive percent agreement = [Number of ARCHITECT Anti-HCV reactive results with the *HCV Infected* status] x 100%
[Total number of *HCV Infected* status]

Negative percent agreement = [Number of ARCHITECT Anti-HCV nonreactive results with the *HCV Not Infected* status] x 100%
[Total number of *HCV Not Infected* status]

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Analytical Specificity

The ARCHITECT Anti-HCV assay was evaluated for potential cross-reactivity for specimens from individuals with medical conditions unrelated to HCV infection. The specimens were tested using the ARCHITECT Anti-HCV assay and the comparator anti-HCV assay. The final results for each of the specimens were compared between the two assays. The data are summarized in the following table.

Reactivity of the ARCHITECT Anti-HCV Assay in Individuals with Medical Conditions Unrelated to HCV Infection

		Comparator Anti-HCV Assay								
		Nonreactive			Equivocal			Reactive[a]		
		ARCHITECT Anti-HCV			ARCHITECT Anti-HCV			ARCHITECT Anti-HCV		
Category	n	NR[b]	EQ[b]	R[b]	NR[b]	EQ[b]	R[b]	NR[b]	EQ[b]	R[b]
Cytomegalovirus (anti-CMV positive)	10	10	0	0	0	0	0	0	0	0
Epstein-Barr Virus (anti-EBV positive)	10	10	0	0	0	0	0	0	0	0
Hepatitis A Virus (anti-HAV positive)	10	8	0	0	1[c]	0	0	0	0	1
Hepatitis B Virus (anti-HBV positive)	10	10	0	0	0	0	0	0	0	0
Human Immunodeficiency Virus (anti-HIV-1 positive)	10	6	0	0	0	0	0	1[c]	0	3
Anti-Nuclear Antibody (ANA)	10	10	0	0	0	0	0	0	0	0
Escherichia coli (E. Coli)	3	3	0	0	0	0	0	0	0	0
Elevated IgG	10	9	0	0	0	0	0	0	0	1
Elevated IgM	10	8	0	0	0	0	0	0	0	2
Elevated total bilirubin	10	4	0	0	0	0	0	0	0	6
Elevated total protein	8	5	0	0	0	0	0	0	0	3
Herpes Simplex Virus (HSV) IgG	5	5	0	0	0	0	0	0	0	0
Human T-cell Lymphotropic Virus (HTLV)	10	10	0	0	0	0	0	0	0	0
Human Anti-Mouse Antibodies (HAMA) positive	10	10	0	0	0	0	0	0	0	0
Influenza vaccine recipients	10	9	0	0	0	0	0	0	0	1
Multiparous female	10	10	0	0	0	0	0	0	0	0
Non-viral liver disease	10	10	0	0	0	0	0	0	0	0
Rheumatoid factor positive	10	10	0	0	0	0	0	0	0	0
Rubella	10	10	0	0	0	0	0	0	0	0
Syphilis	10	6	0	0	0	0	0	1[e]	0	3
Systemic Lupus Erythematosus (SLE)	4	4	0	0	0	0	0	0	0	0
Toxoplasmosis IgG positive	9	9	0	0	0	0	0	0	0	0
Varicella Zoster Virus (VZV) positive	10	9	0	0	0	0	0	0	0	1
Yeast infection	9	9	0	0	0	0	0	0	0	0
Total	**218**	**194**	**0**	**0**	**1**	**0**	**0**	**2**	**0**	**21**

[a] Each reactive anti-HCV result was verified using the comparator anti-HCV assay.

[b] NR = Nonreactive, EQ = Equivocal, R = Reactive

[c] The final result of the anti-HAV positive specimen was anti-HCV negative when tested using the Chiron RIBA HCV 3.0 SIA and HCV RNA negative when tested using the Roche COBAS AMPLICOR HCV Test v2.0.

[d] The final result of the anti-HIV-1 positive specimen was anti-HCV indeterminate when tested using the Chiron RIBA HCV 3.0 SIA and HCV RNA negative when tested using the Roche COBAS AMPLICOR HCV Test v2.0.

[e] The final result of the syphilis specimen was anti-HCV negative when tested using the Chiron RIBA HCV 3.0 SIA and HCV RNA negative when tested using the Roche COBAS AMPLICOR HCV Test v2.0.

Interference

At the concentrations listed below, bilirubin (conjugated and unconjugated), hemoglobin, total protein, and triglycerides showed less than 10% interference in the ARCHITECT Anti-HCV assay for high negative samples (S/CO range: 0.60 to 0.99) and low positive samples (S/CO range: 1.00 to 1.40):

- Bilirubin ≤ 20 mg/dL
- Hemoglobin ≤ 500 mg/dL
- Total Protein ≤ 12 g/dL
- Triglycerides ≤ 3000 mg/dL

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Tube Type Matrix Comparison

The following tube types are acceptable for use with the ARCHITECT Anti-HCV assay:

- Glass: serum and serum separator
- Plastic: serum, serum separator, lithium heparin plasma separator, sodium heparin, and dipotassium EDTA

On average, the tube types listed in the table below showed less than a 10% difference when compared to the control tube type (glass serum) for high negative samples (S/CO range: 0.60 to 0.99) and low positive samples (S/CO range: 1.00 to 1.40).

With the tube types listed in the table below, the ARCHITECT Anti-HCV assay showed the following distribution of percent differences when compared to the glass serum tube type.

Tube Type	Distribution of the differences		
	< 10%	≥ 10% to ≤ 20%	> 20%
Glass Serum Separator	85.0%(34/40)	15.0%(6/40)	-
Plastic Serum	95.0%(38/40)	5.0% (2/40)	-
Plastic Serum Separator	90.0%(36/40)	7.5%(3/40)	2.5%(1/40)
Plastic Lithium Heparin Plasma Separator	72.5%(29/40)	22.5%(9/40)	5.0%(2/40)
Plastic Sodium Heparin	75.0%(30/40)	22.5%(9/40)	2.5%(1/40)
Plastic Dipotassium EDTA	72.5%(29/40)	20.0%(8/40)	7.5%(3/40)

Seroconversion Panels

The ARCHITECT Anti-HCV assay detects the same or greater overall number of reactive bleeds as the comparator anti-HCV assay. Nineteen anti-HCV patient seroconversion panel sets were obtained from two commercial vendors and tested using the ARCHITECT Anti-HCV assay and the comparator anti-HCV assay. For members of panels that had a reactive status in the ARCHITECT Anti-HCV assay earlier than in the comparator anti-HCV assay, supplemental testing with the Chiron RIBA HCV 3.0 SIA and the Roche COBAS AMPLICOR HCV Test v2.0 was performed on the reactive panel members. The data are summarized in the following table.

ARCHITECT Anti-HCV Assay
Days to Evidence of HCV Infection
Seroconversion Panels

	Comparator Anti-HCV assay			ARCHITECT Anti-HCV assay			Chiron RIBA HCV 3.0 SIA			Roche COBAS AMPLICOR HCV Test v2.0		Difference in Days to Anti-HCV Reactive Results Comparator - ARCHITECT[b]
Panel ID	NR[a]	EQ[a]	R[a]	NR[a]	EQ[a]	R[a]	-	IND[a]	+	-	+	
PHV904	7	9	14	7		9	9				9	5
PHV905	11	14	18	7		11	11	14			11	7
PHV906			0			0	--	--	--	--	--	0
PHV907	13		18	13		18	--	--	--	--	--	0
PHV908	11	13	19	5		11	11	13			11	8
PHV909	30		***	0		28		30			28	***
PHV910	4		8	4		8	--	--	--	--	--	0
PHV911	3		14	3		14	--	--	--	--	--	0
PHV912	4		7	4		7	--	--	--	--	--	0
PHV914	19		24	12		16		19			16	8
PHV916	9	16	19	9		16	16				16	3
PHV917	22		85	22		85	--	--	--	--	--	0
PHV918	16		24	16		24	--	--	--	--	--	0
PHV920	7	13	16	7		13	13				13	3
HCV 6212	0		12	0		12	--	--	--	--	--	0
HCV 6213	35		37	35		37	--	--	--	--	--	0
HCV 6214	23		25	25		30	--	--	--	--	--	-5
HCV 6216	17	23	***	17		23		23		23		***
HCV 6229	10	17	20	10		17	17				17	3

[a] NR = Nonreactive, EQ = Equivocal, R = Reactive, IND = Indeterminate

[b] The dates of the first reactive test results were compared in the comparator assay and ARCHITECT Anti-HCV assay. If the first reactive test result occurred on the same day, then the difference is 0; if ARCHITECT Anti-HCV assay had an earlier date, then the difference is positive; if ARCHITECT Anti-HCV assay had a later date, then the difference is negative.

*** The panel never seroconverted from a nonreactive status to a reactive status with the comparator anti-HCV assay. Supplemental testing was not performed.

Genotype Detection

The ARCHITECT Anti-HCV assay detects the same commonly recognized genotypes of HCV as the comparator anti-HCV assay. Two lots of genotype panels were obtained from Teragenix Corporation which consisted of the following genotypes, as determined by the vendor: 1a, 1b, 1c, 2, 2a, 2b, 2c, 3a, 3b, 4, 4a, 4c, 4d, 5, 5a, and 6a. The lots were tested using the ARCHITECT Anti-HCV assay and the comparator anti-HCV assay, and the final results were compared. The ARCHITECT and the comparator anti-HCV assay final results were in 100% agreement for the genotypes of HCV.

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The following U.S. Patents are relevant to the ARCHITECT System or its components. There are other such patents and patent applications in the United States and worldwide.

5 468 646	5 543 524	5 545 739
5 565 570	5 669 819	5 783 699

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Manufactured for
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by
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June 2006

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ARCHITECT®
SYSTEM

In Vitro Test
REF 1L79-01
34-4150/R1

Anti-HCV

Calibrator

Key to symbols used

REF	List Number	LOT	Lot Number
IVD	*In Vitro* Diagnostic Medical Device		Expiration Date
2°C–8°C	Store at 2-8°C	CAL 1	Calibrator 1
	CAUTION: Consult accompanying documents		

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INTENDED USE

The ARCHITECT Anti-HCV Calibrator is used for the calibration of the ARCHITECT *i* System when the system is used for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to hepatitis C virus (anti-HCV) using the ARCHITECT Anti-HCV Reagent Kit. The performance of the ARCHITECT Anti-HCV Calibrator has not been established with any other anti-HCV assays.

PRINCIPLES OF THE PROCEDURE

The ARCHITECT *i* System calculates the cutoff Relative Light Units (RLU) from the mean chemiluminescent signal of three Anti-HCV Calibrator 1 replicates. The acceptability of the calibration is assessed against a parameter. If the calibration is acceptable, the cutoff RLU is calculated by multiplying the Anti-HCV Calibrator 1 mean RLU by 0.074.

Cutoff RLU = Calibrator 1 Mean RLU x 0.074

The acceptable calibration is stored by the ARCHITECT *i* System for use with any reagent kit of that lot. The calibration should be used in conjunction with control ranges to determine the validity of the calibration.

WARNINGS AND PRECAUTIONS

- For *In Vitro* Diagnostic Use.
- **CAUTION: This product contains human sourced infectious and/or potentially infectious components. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens,[1] Biosafety Level 2[2] or other appropriate biosafety practices[2-4] should be used for materials that contain or are suspected of containing infectious agents.**
- The calibrator is reactive for anti-HCV and nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, and anti-HIV-1/HIV-2. Reactive plasma is heat-inactivated.
- This product contains sodium azide. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.

MATERIALS PROVIDED

1 Bottle (4 mL) ARCHITECT Anti-HCV Calibrator 1 is recalcified, heat-inactivated anti-HCV positive human plasma in recalcified anti-HCV negative human plasma. Calibrator 1 is green and contains Acid Yellow No. 23 and Acid Blue No. 9 dyes. Preservative: sodium azide.

STANDARDIZATION

Calibrator 1 is traceable to an Abbott internal reference standard. This internal reference standard is manufactured by diluting anti-HCV reactive recalcified human plasma with anti-HCV nonreactive recalcified human plasma.

PREPARATION AND STORAGE

- The calibrator is liquid ready-to-use. No preparation is required.
- When stored and handled as directed, the calibrator is stable until the expiration date.
- The calibrator must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- Refer to the ARCHITECT Anti-HCV assay reagent package insert for the maximum on board stability requirements.

Store at 2-8°C

QUALITY CONTROL PROCEDURES

Refer to the ARCHITECT Anti-HCV assay reagent package insert and ARCHITECT System Operations Manual for additional information.

A single sample of each control level must be tested to evaluate the assay calibration. For information on ordering controls, refer to the ARCHITECT System Operations Manual, Section 5.

- Ensure that assay control values are within the ranges specified in the control package insert.

Once an ARCHITECT Anti-HCV calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:

- A reagent kit with a new lot number is used.
- Controls are out of range

PROCEDURE

- ARCHITECT Anti-HCV Calibrator 1 must be mixed by gentle inversion before use.
- To perform a calibration, test ARCHITECT Anti-HCV Calibrator 1 in triplicate. The calibrator should be priority loaded.
- To obtain the recommended volume requirements for the ARCHITECT Anti-HCV Calibrator 1, hold the bottle **vertically** and dispense 5 drops into the respective sample cup.
- For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Occupational exposure to bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 4th ed. Washington, DC: US Government Printing Office; May 1999.
3. World Health Organization. *Laboratory Biosafety Manual*. Geneva: World Health Organization; 2004.
4. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline—Third Edition*. CLSI Document M29-A3. Wayne, PA: CLSI: 2005.

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Manufactured for
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by
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ARCHITECT® SYSTEM

In Vitro Test
REF 1L79-10
34-4151/R1

Anti-HCV

Controls

Key to symbols used

REF	List Number	LOT	Lot Number
IVD	*In Vitro* Diagnostic Medical Device		Expiration Date
2°C–8°C	Store at 2-8°C	CONTROL –	Negative Control
	CAUTION, Consult accompanying documents	CONTROL +	Positive Control
		TITER ≥	Minimum Titer

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INTENDED USE

The ARCHITECT Anti-HCV Controls are used for monitoring the performance of the ARCHITECT *i* System when used for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to hepatitis C virus (anti-HCV) when using the ARCHITECT Anti-HCV Reagent Kit. The performance of the ARCHITECT Anti-HCV Controls has not been established with any other anti-HCV assays.

WARNINGS AND PRECAUTIONS

- **For *In Vitro* Diagnostic Use.**

⚠ CAUTION: This product contains human sourced infectious and/or potentially infectious components. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens,[1] Biosafety Level 2[2] or other appropriate biosafety practices[3,4] should be used for materials that contain or are suspected of containing infectious agents.

- The negative control is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.
- The positive control is reactive for anti-HCV and nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, and anti-HIV-1/HIV-2. Reactive plasma is heat-inactivated.
- This product contains sodium azide. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.

MATERIALS PROVIDED

2 Bottles (8 mL each) ARCHITECT Anti-HCV Controls (1 bottle of negative control and 1 bottle of positive control).

- The negative control is recalcified human plasma. Preservative: sodium azide.
- The positive control is recalcified, heat-inactivated anti-HCV positive human plasma in recalcified anti-HCV negative human plasma. The positive control is blue and contains Acid Blue No. 9 dye. Preservative: sodium azide.

PREPARATION AND STORAGE

- Controls are liquid ready-to-use. No preparation is required.
- When stored and handled as directed, the controls are stable until the expiration date.
- The controls must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- Refer to the ARCHITECT Anti-HCV assay reagent package insert for the maximum on board stability requirements.

Store at 2-8°C

QUALITY CONTROL PROCEDURES

Refer to the ARCHITECT Anti-HCV assay reagent package insert and ARCHITECT System Operations Manual for additional information.

The recommended control requirement for the ARCHITECT Anti-HCV assay is that a single sample of each control level be tested once every 24 hours each day of use. Additional controls may be tested in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

PROCEDURE

- ARCHITECT Anti-HCV Controls must be mixed by gentle inversion before use.
- To obtain the recommended volume requirements for the ARCHITECT Anti-HCV Controls, hold the bottles **vertically** and dispense 6 drops of each control into each respective sample cup.
- For information on ordering patient specimens and the positive control and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Use the following instructions to order an ARCHITECT Anti-HCV Negative Control (nonreactive for anti-HCV):
  - Order the negative control as a patient sample. The negative control cannot be ordered as a Control.
  - For the negative control, do not configure or use the Westgard or Levey-Jennings software screens for quality control analysis. The use of these screens for the negative control will result in data that is not statistically valid.
  - Manual verification of the validity of the negative control is required any time the negative control is run. For control values that fall outside the validity range listed in this package insert, refer to the ARCHITECT *i* System Operations Manual, Section 10 for troubleshooting information.
  - Because the negative control is run as a patient sample, patient values will not be flagged by the ARCHITECT *i* System if a negative control is outside of its control range. Only release patient results if a valid negative control value is obtained.
- To troubleshoot control values that fall outside the control range, refer to the ARCHITECT System Operations Manual, Section 10.

EXPECTED RESULTS

The controls must fall within the following ranges:

Control	Color	Titer	Range (S/CO)
CONTROL -	Natural	N/A	< 0.60
CONTROL +	Blue	1:1	193 - 5.35

Note: The insert ranges for the controls are not lot specific and represent the total range of values which may be generated throughout the life of the product. It is recommended that each laboratory establish its own means and acceptable ranges which should fall within the package insert ranges. Sources of variation that can be expected include:

- Calibration
- Control lot
- Instrument
- Calibrator lot
- Reagent lot

LIMITATIONS

- Control values have not been established for assays other than the ARCHITECT Anti-HCV assay. If the user wishes to use this control material with other assays, it is their responsibility to establish the appropriate ranges.
- The ARCHITECT Anti-HCV Controls are in a serum matrix made from recalcified plasma. The user should provide alternate control material for plasma when necessary.
- The controls are not calibrators and should not be used for assay calibration.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Occupational exposure to bloodborne pathogens.
2. US Department of Health and Human Services, *Biosafety in Microbiological and Biomedical Laboratories*, 4th ed. Washington, DC: US Government Printing Office: May 1999.
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